

It is usually thought that favism does not occur in people of Anglo-Saxon origin. So far as we know, this is the second case to be reported in English families. A third family is being investigated by Davies (1961), together with that of the first patient described by McCarthy (1955). It is probable that further cases of favism are occurring in this country, but that the diagnosis will not be made unless the patient is questioned about broad beans. These will be in season here shortly, although, with the introduction of frozen food, the condition may occur at other times of the year (Gower and Frommer, 1960).

In a typical case there are early symptoms of headache, dizziness, diarrhoea, and vomiting. After a variable period of up to two days, acute haemolysis ensues with jaundice, anaemia, and haemoglobinuria. There is a pronounced reticulocytosis and leucocytosis, with a normal red-cell osmotic fragility and a negative Coombs antiglobulin test.

It is now possible to confirm the diagnosis directly by estimating glucose-6-phosphate dehydrogenase in the red cells. Defective red cells may also be detected by a glutathione-stability test (Beutler, 1957) or by the "Heinz body test." The last presents no technical difficulty and appears to be suitable for routine laboratory use.

In most reported cases in adults there is a rapid recovery from the haemolytic episode; but in children the disease is more serious, with a mortality rate up to 10% (Luisada, 1941). However, blood transfusion is often necessary, and in addition to correcting red-cell loss it may have some specific effect through the protective action of normal plasma (Roth and Frumin, 1960). Cortisone and antihistamine drugs are often given, although their value is uncertain.

SUMMARY

A case of favism in an Englishwoman with no known foreign antecedents is reported.

The genetic abnormality of glucose-6-phosphate dehydrogenase deficiency has been found in the erythrocytes of the patient and members of her family.

It is suggested that further cases may be occurring unrecognized in Britain, and the diagnosis is discussed.

We are indebted to Dr. H. Lehmann and to Dr. B. A. L. Hurn for carrying out the enzyme estimations, and to Dr. T. A. J. Pranker for confirming the absence of the enzyme in the patient's erythrocytes.

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Medical Memoranda

17265 Aplastic Anaemia Due to Treatment with Potassium Perchlorate

Antithyroid drugs are widely used as the initial or as the only treatment for hyperthyroidism. The choice of antithyroid drug has rested largely on the incidence of minor or severe side-effects encountered in its use. Potassium perchlorate has been increasingly used as it is effective and inexpensive, and has been thought to have a low incidence of minor side-effects. Major blood dyscrasias have not been reported with low dosage.

A case of aplastic anaemia is reported in a patient who never received a dose larger than 800 mg. of potassium perchlorate a day.

CASE HISTORY

The patient was first seen in 1947 at the age of 38 with symptoms and signs typical of thyrotoxicosis. She was treated with methylthiouracil followed by partial thyroidectomy. She regained the 28 lb. (12.7 kg.) in weight she had lost, and subsequently enjoyed good health until 1957. In 1957 she noticed increasing nervousness, irritability, and discomfort in her wrists and shoulders. In 1959, although continuing her work as a clerk, she lost 35 lb. (15.9 kg.) in weight, and complained of nervousness, irritability, tremor, increased sweating, and dislike of hot weather.

On examination in July, 1959, she was thin, and weighed 6 st. 6 lb. (40.8 kg.). The circulation was overactive, with a fast pulse and blood-pressure 160/60. There was a fine tremor of the fingers with swelling of proximal interphalangeal joints and pain and limitation of movement in both shoulders. There was slight proptosis of both eyes and bilateral lid-lag. The right lobe of the thyroid was enlarged and vascular.

Investigations. — B.M.R. +43%. Radioiodine urinary excretion reduced, T index -31.2 (normal 3-14). Blood: haemoglobin 80%, normal white count, E.S.R. 56 mm./hr. (Westergren). Differential agglutination test 1:64. Latex fixation + + +. X-ray examination of hands: joints show changes compatible with early rheumatoid arthritis.

A diagnosis of (1) recurrent hyperthyroidism and (2) early rheumatoid arthritis was made.

Treatment.—Prednisolone, 20 mg. daily was given for one week, and the dose was then gradually reduced to 5 mg. twice daily six weeks later, and subsequently continued at this dose until her final admission. Potassium perchlorate, 200 mg. four times daily, was given for 14 weeks, the dose being then reduced to 200 mg. three times daily until her final admission. The total period of treatment on potassium perchlorate was 33½ weeks. The response to treatment was dramatic. She gained 28 lb. (12.7 kg.) in weight, lost all signs and symptoms of hyperthyroidism, and enjoyed normal and painless use of her joints. Fourteen weeks after starting treatment with potassium perchlorate the palpable right lobe of the thyroid appeared slightly enlarged and there was some puffiness of the face compatible with mild thyroid deficiency. At this time triiodothyronine, 0.02 mg. three times daily, was given for 12 weeks in addition to the potassium perchlorate. No features suggestive of hypothyroidism were evident after the fourteenth week of initiating treatment with potassium perchlorate, and the patient noted no gastro-intestinal or other side-effects.

Final Admission.—About April 10, 1960, after 32½ weeks of antithyroid treatment, she felt well, but noticed some spots on her skin. On April 18 she was referred with severe epistaxis to a casualty department and was admitted the next day. On admission her temperature was 101° F. (38.3° C.) and pulse 120. She was pale, with a purpuric rash on her chest and arms, and tender enlarged lymph

nodes in the neck. Blood: haemoglobin 63%; W.B.C. 2,900 (98% lymphocytes, 2% polymorphs); platelets 20,000; bleeding-time (Duke) 30 minutes; coagulation time 4 minutes. Sternal marrow (April 20): complete absence of erythropoietic and granulopoietic cells and of megakaryocytes. The cells present were mostly lymphocytes and plasma and reticulum cells; and the marrow picture was typical of aplastic anaemia. In her final illness the patient was treated with penicillin, streptomycin, fresh blood transfusion, and steroids; but she died five days later with signs of severe pulmonary infection.

Post-mortem Examination.—The body was adequately nourished and slightly jaundiced, with scattered purpuric spots. There were scattered petechiae on the pericardium and on mucous membranes, with haemorrhagic consolidation in the lungs and pleurisy on the surface of the lower lobes. The spleen was firm and dark, the marrow of vertebrae appeared normal, but the femoral marrow was pale. The right lobe of the thyroid was slightly enlarged.

COMMENT

The evidence suggests that, in this patient, aplastic anaemia was due to the treatment with potassium perchlorate. The steroid therapy might have obscured the onset of symptoms resulting from toxic action on the marrow or it might possibly have contributed to its development. Corticosteroid therapy is usually regarded as being of value in the treatment of aplastic anaemia, although aplastic anaemia has been attributed to corticotrophin injections (Snively *et al.*, 1953) and agranulocytosis has been attributed to prednisolone (Rokseth, 1960). We have encountered no other serious side-effects in the treatment of some 50 patients with potassium perchlorate alone. One patient receiving both carbimazole and potassium perchlorate developed agranulocytosis.

A woman of 48 presented with a two-year history of marked loss of weight, dyspnoea, and auricular fibrillation, and with a massive vascular and nodular goitre estimated to weigh 300 g. She had had a partial thyroidectomy for hyperthyroidism 20 years before and had delayed seeking treatment as she feared a further operation. In view of her massive goitre she was thought unsuitable for surgery and was given carbimazole 15 mg. three times daily and potassium perchlorate 200 mg. three times daily; her cardiac condition was controlled with digoxin. She improved rapidly, but after 30 days' treatment became seriously ill with a sore throat, fever, and a peripheral blood count typical of agranulocytosis; a sternal marrow biopsy done some days later showed appearances compatible with recovering agranulocytosis. On withdrawal of antithyroid drugs and treatment with antibiotics, potassium iodide, and blood transfusion she recovered, and was later treated satisfactorily with radioiodine therapy.

Carbimazole was given to this patient in dosage larger than average on account of her severe disease and massive goitre, and may therefore be the most suspect toxic agent in this case. Serious blood dyscrasias are uncommon when carbimazole is administered in doses of 30 mg. daily or less (Burrell *et al.*, 1956). But we have seen one death from agranulocytosis in a woman of 52 treated for hyperthyroidism with carbimazole in a dose of 30 mg. daily for five weeks.

Although agranulocytosis is a well-known complication of antithyroid drug treatment, aplastic anaemia has been seldom recorded and has not previously been attributed to potassium perchlorate in any report in the medical press.

Aplastic anaemia due to treatment with carbimazole was reported by Richardson *et al.* (1954) and by Burrell (1956) with fatal outcome in both patients. Aplastic

anaemia due to treatment with methimazole, from which the patient recovered, was reported by Levine and Rosenberg (1954).

It would seem possible that aplastic anaemia may occur especially in patients in whom the recognition of the toxic side-effects has been delayed and the drug has not been promptly withdrawn.

The occurrence of aplastic anaemia in our patient suggests that this condition may be encountered in future with the more widespread use of potassium perchlorate as an antithyroid agent. Although when doses smaller than 1,000 mg. daily are used toxic side-effects are thought to be uncommon (Crooks and Wayne, 1960; Morgans and Trotter, 1960), further experience may reveal that small doses are occasionally hazardous.

Even after repeated verbal warnings concerning the possible side-effects of antithyroid agents, intelligent patients may fail to report for blood examination as they have been requested to do in the event of ill-health. A suitably worded card and a clearly labelled container stating the details of the drug being taken might help the patient and practitioner.

The early recognition of the toxic side-effects and the prompt withdrawal of the drug may contribute to avoiding the serious toxic effects.

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Fatal Aplastic Anaemia after Treatment of Thyrotoxicosis with Potassium Perchlorate

Experience during the past six years has shown potassium perchlorate to be as effective an antithyroid agent as the more commonly used organic drugs methylthiouracil and carbimazole (Morgans and Trotter, 1954; Godley and Stanbury, 1954; Smellie, 1957; Fairhurst and Hollingworth, 1958; Crooks and Wayne, 1959; Cook and Hawe, 1960; *Brit. med. J.*, 1960). The incidence of serious side-effects so far reported from its use has been low, and includes only two cases of agranulocytosis, each of which recovered, but the occurrence of a related aplastic anaemia has not hitherto been described.

CASE REPORT

A woman aged 29 presented with characteristic signs of thyrotoxicosis of moderate severity, confirmed by radioactive iodine studies using a diagnostic dose of 25 microcuries. No history of previous blood disease was given, and although no blood count was done at this stage her mucous membranes were of normal colour.

Treatment was begun with oral potassium perchlorate 1 g./day, given as 400 mg. morning and evening and 200 mg. midday. A month later she showed clinical improvement of thyrotoxic features, so the drug was continued in the same dosage for a further two months. At her next attendance she had gained 7 lb. (3.175 g.) in weight, but complained of fatigue and generalized aching pains; she had a mildly myxoedematous appearance, so the dosage was

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